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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,887	07/30/2002	Jurgen Engel	103832-512-NP	6290

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EXAMINER	
GALVEZ, JAMES JASON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,887	ENGEL ET AL.	
	Examiner	Art Unit	
	J. Jason Galvez	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/05/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1 and the species Cetrorelix in the reply filed on 10/01/2004 is acknowledged. Amendments to the claims were presented in Applicant's response to the election/restriction requirement wherein claims 7-11 were withdrawn and the addition of claims dependent on Group 1 that are considered to be a part of the invention were presented. Therefore, the claims examined include the original claims 1-6 and the newly presented claims 12-16 with the elected species Cetrorelix.

Specification

The use of the trademark CETRORELIX, TEVERELIX, ANTIDE, AND ABARELIX has been noted in this application. A trademark should be capitalized wherever it appears and should be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986)); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of administering LHRH in the treatment of BPH and endometriosis, does not reasonably provide enablement for a method of administering LHRH in a treatment of any disease or to enhance an immune response to an antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The recitation that the method can be utilized to modify the T-cell population in an individual "suffering from a disease" is not fully supported by the disclosure. The Examiner has interpreted the claim to mean that the claimed invention can be used in the treatment of any disease. The broad assertion implies that the method could be used for any disease that coincides with altered T-cell activity, e.g. inflammation, such diseases range from heart attacks to inflammatory bowel disease. Based on the limited disclosure it would not be possible to know if the method can be used in the myriad of diseases that are implicit to the claim. Applicant also never discloses any data or even

speculative remarks regarding LHRH antagonists and the ability to enhance an immune response to an antigen. Furthermore, there are a tremendous number of antigens that may or may not respond to LHRH antagonists even if Applicant substantiated the claim of enhanced immune response to an antigen using LHRH.

Therefore, a person of ordinary skill in the art would not be able to practice the invention commensurate in scope due to the quantity of experimentation necessary, the absence of working examples, the nature of the invention, the state of the prior art, and the breadth of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to decreased sex hormone levels "to a certain extent". Although the "certain extent" is qualified to a level that is not below castration, it is not clear what a certain extent encompasses. For example, does "to a certain extent" represent levels that are 95%, 90%, 85%, 80%, etc. of basal levels? Accordingly, the claim is unclear regarding what a "certain extent" is and thus, is indefinite.

Claims 2-6 are drawn to consequences of lowered sex hormone levels wherein a "modification of the T-cell population" is the result. Does this modification entail an upregulation or downregulation? Or is there a change in the number of certain T-cells

subtypes (e.g. helper T-cells vs. regulatory T-cells)? It is unclear to the Examiner what "a modification of the T-cell population" means. Thus, the claims are indefinite.

Claims 14-16 are drawn to a dosing regimen wherein the administration of LHRH is "divided" throughout a period. How will the compounds be divided throughout the treatment? It is unclear how Applicant will be performing dosing schedules. Thus, the claims are indefinite.

Claims 14-16 are drawn to administration of LHRH based on "needs" and "as needed". The use of "needs" and "as needed" is vague and indefinite. How does Applicant define the "needs" of the recipient of the claimed invention? Similarly, How does Applicant define using the method of the claimed invention "as needed"? It is unclear what Applicant means in the recitation of "needs" and "as needed". Thus, the claims are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by prompt Engel et al. (WO 98/10781 [03-98]). Engel et al. teach a method for treating BPH and prostate cancer using the LHRH antagonist Cetrorelix. Engel et al. teach that Cetrorelix is efficacious in the treatment of BPH, wherein the treatment did not drop

hormone levels below the level of castration (Figure 1). In addition to the results of Engel et al. LHRH antagonist have inherent properties that were not explicitly disclosed. Inherent properties are present within a method or a compound whether these properties have been previously disclosed, therefore inherent properties do not need to be explicitly disclosed to meet all of the limitations of the claims. In the instant case, LHRH antagonists inherently have the ability to modify T-cell populations.

The ability of LHRH antagonists, like Cetrorelix, to modify T-cells populations is an inherent property that is exemplified by the finding of Zakharova et al. (Biochemistry (Mosc.), Vol. 65(10): pp. 1135-1139 [10/2000]). Zakharova et al. teach that LHRH antagonists can decrease thymocyte (T-cell) proliferation (Figure 1 and Figure 3). Regarding dosing regimen, Engel et al. teach specific doses that encompass the claimed doses in the in instant invention (p. 6: lines 15-18).

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Zakharova et al. (Biochemistry (Mosc.), Vol. 65(10): pp. 1135-1139 [10/2000]). Zakharova et al. teach that LHRH antagonists can decrease thymocyte (T-cell) proliferation (Figure 1 and 3). While there was no mention of inherent properties, such as lowering hormone levels, these properties are still present.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dubernard et al. (Diabetes and Metabolism (Paris), Vol. 24: pp. 195-199 [1998]) in view of Zakharova et al. (Biochemistry (Mosc.), Vol. 65(10): pp. 1135-1139 [10/2000]). Dubernard et al. teach that immunosuppression has increased outcomes associated with transplantation, i.e. a decreased chance of host versus graft rejection (p. 196: paragraph 1). However, there is no teaching of the use of LHRH antagonists to reduce immune response following organ transplantation.

Zakharova et al. teach that LHRH antagonists are able to decrease thymocyte (T-cell) proliferation (Figure 1 and Figure 3).

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Debernard et al. and Zakharova et al to develop a method of decreasing host versus graft rejection using LHRH antagonists. A person of ordinary skill in the art would have been motivated to combine the teachings because Debernard et al. teach that immunosuppression is a useful method of treating host versus graft rejection, and Zakharova et al. teaches a method for obtaining this result, i.e. decreased

T-cell proliferation and consequently decreased immune response. Furthermore, the expectation of success is reasonably assured based on the findings of Zakharova et al. that showed a significant decrease in T-cell proliferation following stimulation, which is a similar scenario encountered in transplantation of organs with the foreign organ acting to stimulate the proliferation of T-cells.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-14 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-11 of copending Application No. 10/717,129. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **J. Jason Galvez, Ph.D**. whose telephone number is

571-272-2935. The examiner can normally be reached Monday through Friday 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached at **571-272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JJG
11/16/2004